Scientific Abstract

Squamous cell carcinoma of the head and neck has an annual incidence of approximately 42,000 patients per year in the United States, and the median survival time for patients with local or disseminated recurrent disease has been reported as 6 months, with 20% of patients surviving at 1 year. There is evidence that the poor prognosis in patients with advanced head and neck cancer may be associated with alterations in humoral and cellular immunity, and therefore therapy with immunomodulators such as the interferons and interleukins may be beneficial in treatment of this advanced disease. Interferon-alpha (IFN-α) is known to have antiviral, antiproliferative, immunoregulatory, and antiangiogenic properties. The recombinant protein has been approved for use in many clinical indications, including hairy cell leukemia, chronic hepatitis B and C, Kaposi's sarcoma, and chronic myelogenous leukemia.

In animal models, the partial or complete regression of several types of tumors has been observed following direct intratumoral administration of IFN-α Gene Medicine, a non-viral gene therapy consisting of a plasmid which expresses human interferon-alpha 2b formulated with the synthetic polymer polyvinylpyrrolidone in saline. When administered intratumorally to tumor-bearing mice, IFN-α Gene Medicine leads to a decrease in the rate of tumor progression, with complete tumor regression in some cases. In cases where tumor rejection occurs, the animals also demonstrate immunity to re-challenge with the same tumor cell type. These data suggest that administration of the IFN-α Gene Medicine leads to the generation of an anti-tumor immune response. It is anticipated that the anti-tumor immune response will promote tumor regression, inhibition of tumor progression, and/or prevention of metastasis in humans.

The clinical studies proposed are directed at expressing human IFN-α at a tumor site by non-viral, polymer-mediated delivery of a gene encoding IFN-α. This gene transfer is intended to induce local (intra- or peri-tumoral) expression of IFN-α at levels sufficient to promote an anti-tumor response without high systemic concentrations of IFN-α protein. In animal experiments conducted to address this particular safety issue, a concentration of IFN-α plasmid DNA sufficient to bring about an anti-tumor response did not lead to significant systemic levels of the protein. In addition, preclinical toxicology testing in nonhuman primates demonstrated the absence of side-effects of IFN-α Gene Medicine through the highest dose tested, 12 mg/kg. This offers a distinct advantage in that the likelihood of occurrence of side-effects observed after high dose systemic IFN-α treatment should be greatly reduced, if not eliminated.